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BRIEF REPORT

Infective Endocarditis: How Do We Currently Interpret the Duke Minor Criterion "Predisposing Heart Condition" in Native Valves?

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ABSTRACT

Introduction: The term "predisposing heart condition" is used as an indication of antimicrobial prophylaxis to prevent infective endocarditis (IE) and as a criterion for diagnosing IE according to modified Duke criteria. The purpose of this survey was to elaborate clinician's knowledge and opinion on relevant heart conditions as a Duke minor criterion for the diagnosis of IE.

Methods: A questionnaire was created that consisted of two knowledge and two opinion questions on the term predisposing heart condition. The survey included results from 318 questionnaires with responses from specialists in the field of internal medicine, infectious diseases, and cardiology.

Results: The answers of what participants believed to be currently a Duke minor criterion and what they thought should be minor criterion were very distributed with a median accordance of 33%.

Conclusion: The survey indicates that there is significant uncertainty regarding what is encountered as a Duke minor criterion predisposing heart condition in a native valve.

Keywords: Endocarditis; Risk assessment; Valvular heart disease

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INTRODUCTION

The original concept of antibiotic prophylaxis for infective endocarditis (IE) led to the

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recommendation for antimicrobial agents in a large number of patients with predisposing cardiac conditions who were undergoing a wide range of procedures. In the following years, indications for antibiotic prophylaxis were restricted and the populations at risk defined. These populations included (1) patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair; (2) patients with a previous episode of IE; and (3) patients with congenital heart disease (CHD). The last group consists of two subcategories: (a) those with any type of cyanotic CHD and (b) those with any type of CHD that has been repaired with prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or for the patient's lifetime if a residual shunt or valvular regurgitation remains [1]. In the modified Duke criteria, on the other hand, a "predisposing heart condition" is a minor criterion for diagnosing IE. In cases of suspected IE but negative imaging results, this criterion may become relevant for forming the diagnosis. Thus, the same term (predisposing heart condition) is used as an indication of antimicrobial prophylaxis to prevent IE and as a criterion for diagnosing IE. However, whereas the use of the term for antimicrobial prophylaxis is (meanwhile) well defined, the criterion for diagnosing IE is not. In our experience, clinicians consider a larger number of heart conditions as a minor criterion for the diagnosis of IE than they use for the prevention of IE [2]. Therefore, we performed a survey to address this impression. The aim of our survey was to elaborate on the knowledge and opinion of clinicians on the applicability of the minor criterion of a predisposing heart condition in native valves for the diagnosis of IE.

METHODS

A questionnaire (Supplemental Material S1) was designed and tested to be completed within 5 min. It included questions about training, degrees, and clinical experience of study participants, as well as two knowledge and two opinion questions. Nineteen departments in 13 different institutions within Switzerland were visited to perform the survey (see "Acknowledgements"). Questionnaires were distributed at morning meetings and directly collected afterwards. All questionnaires were filled out anonymously. A sample size of 300 was targeted prior to the study. Participants included either physicians undergoing postgraduate education and specialization, or specialists in the fields of internal medicine, infectious diseases, or cardiology. Answers were independently evaluated by two members of the study team (A.B. and P.S.) and categorized as acceptable (wide range of answers) or definitely wrong (narrow range of answers, Supplemental Material S2). The rational to accept a wide range of answers relied on the fact that the term "predisposing heart condition" in native valves is not well defined; thus, for many answers it was scientifically difficult to categorize them as definitely wrong. In case of disagreement, a third member of the study team was involved and the decision was made by the majority. Accordance between knowledge and opinion was analyzed and illustrated in a bi-directional graph. For this analysis, foreign body material was excluded because the focus in the opinion question was on native valves, while "foreign body material" was a correct answer in the knowledge question. GraphPad Prism 5.0 was used for statistical analysis. Differences in group proportions were assessed by contingency tables and the Chi-square test, or by Fisher's exact probability test if cell values were less than 5. The Student's *t* test was

applied where appropriate. A two-tailed p value of 0.05 or less was considered significant.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for being included in the study.

RESULTS

Study Participants

In total, 318 questionnaires were collected. We included all of them in the analysis because the completion rate was more than 90%. Less than 5% of the participants had 1–2 years of clinical experience, 19.2% had 2–5 years of experience, and 75.7% had more than 5 years of clinical experience at the time of the survey. Most participants (52%) worked at a secondary care center, 35% at a university hospital (tertiary referral center), and 13% at a regional hospital or in a private practice. The participating centers are listed in the "Acknowledgements". Half of the participants were in postgraduate training for a medical speciality. Of the responders, 31.8% had a double specialization (e.g., internal medicine and cardiology) and 12.9% were undergoing postgraduate training for their second specialization. The majority of participants (61.5%) completed training in general internal medicine. Other frequent specialities included infectious diseases and cardiology. In 91.2% of the responders diagnosis and treatment of IE is part of their routine clinical work.

Questionnaire Answers

Participants were asked whether or not the Duke minor criterion, "predisposing heart condition", is precisely defined in either the European or the American guidelines for IE. Although it is not precisely defined, 54 participants (17.3%) answered yes, 83 (26.6%) answered no, and 175 (56.1%) indicated that they did not know the answer.

Participants were asked what—to their knowledge—a predisposing heart condition is for the diagnosis of IE according to the modified Duke criteria. The most frequent answers are reflected in Table 1. Forty-five participants (14.2%) indicated at least one wrong answer. The proportion of wrong answers did not differ between the specialties (internal medicine 14.2%, cardiology 15.7%, infectious diseases 14.3%, other 15.8%). Similar findings were found when appointment levels were compared for at least one wrong answer (registrars 15.3%, consultants 13.5%, lead physicians 14.3%, and head of departments 11.8%). There was an inverse association between wrong answers and number of years of clinical experience. Thirty percent (30%) of physicians with 1–2 years of experience indicated a least one wrong answer. In doctors with 3–5 years of clinical experience, this proportion was 11.7%, and in doctors with more than 5 years of clinical experience it was 14.3% ($p = 0.02$).

Participants were also asked what—in their opinion—a predisposing heart condition should constitute as a minor criterion for the diagnosis of IE. Although a wide range of answers was given, there was no congruence between knowledge and opinion for the vast majority of the answers (Table 1). The median accordance of the answers to knowledge (question II.1) and opinion (question II.3) for each participant was 33% (SD 38.84%) (Fig. 1). Finally, participants were then presented with a case–control study published in 1982 [3], showing that mitral valve prolapse (MVP) was

Table 1 Frequency of responses to knowledge and opinion questions

Condition	Knowledge question (%)	Opinion question (%)
Foreign body material	67	–[a]
Prior infective endocarditis	32.4	22.9
Valvular vitium	26.1	11.8
Grown-up congenital heart disease	19.0	8.8
Vitium (not specified)	16.3	7.7
Shunt	15.7	13.1
Bicuspid aortic valve	12.7	29.0
Mitral valve insufficiency	12.7	32.3
Mitral valve prolapse	12.1	32.3
Aortic valve stenosis	11.4	31.0
Aortic valve insufficiency	10.1	20.5
Rheumatic heart disease	9.2	12.5
Mitral valve stenosis	8.8	26.6
Cyanotic heart disease	8.2	4.4
Tricuspid valve insufficiency	8.2	17.8
Pulmonary valve insufficiency	6.5	13.5
Tricuspid valve stenosis	5.6	14.5
Degenerative valve disease	5.2	0
Pulmonary valve stenosis	4.6	13.5
Cardiac surgery (without foreign body material)	3.9	4.4
Heart failure	3.3	2.4
Heart transplant	2.9	1.7
Significant turbulence	2.6	2.7
Hypertrophic obstructive cardiomyopathy	1.3	9.1
Dilatative cardiomyopathy	0.3	1.0
Prior myocardial infarction/coronary heart disease	0	1.3
Thrombus	0	0.7
Arrhythmias	0	0.7
Endothelial damage	0	1.0
Low flow	0	0.3
Paravalvular leakage	0	0.3

Table 1 continued

Condition	Knowledge question (%)	Opinion question (%)
Tumor	0	0.3

Participants were asked what they "knew" was a predisposing heart condition for infective endocarditis (knowledge question) and what they felt should be listed as a predisposing heart condition (opinion questions). Results are presented in frequency percentages (%) of the total number of answers

[a] The question focussed in particular on native valves

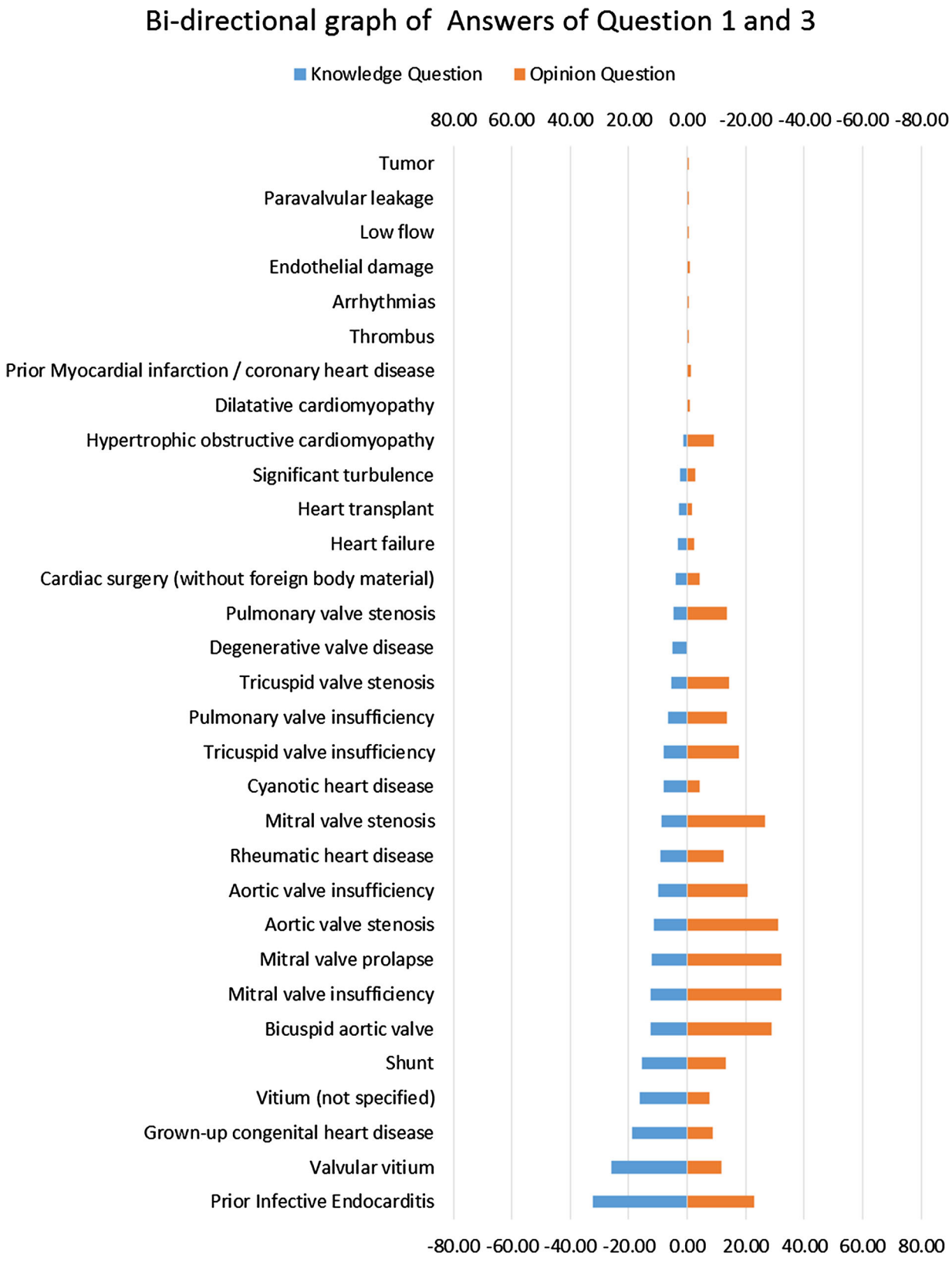
associated with a higher risk for IE (odds ratio 8.2; 95% CI 2.4–28.4). Almost two-thirds of the responders indicated that they would not expect similar results if the study were to be repeated today, either because MVP criteria are different from those used in 1982, or because the echocardiographic technique used today is better than it was in 1982, and thus MVP was previously overdiagnosed.

DISCUSSION

Over the past years, a predisposing heart condition that would put a patient at risk for IE, thus justifying antimicrobial prophylaxis, has been narrowed down to four defined entities. In parallel, diagnostic imaging methods have been improved, and repeated echocardiography for the diagnosis of IE is recommended. Moreover, imaging criterion can be fulfilled by diagnostic means other than echocardiography, including 18F-FDG/PET CT, radiolabelled leukocytes SPECT/CT, and cardiac CT [1, 4]. Nonetheless, the Duke criterion of a predisposing heart condition is poorly defined, in particular for native valves with no history of previous IE. In our survey, the range of answers regarding the nature of a predisposing heart condition was very broad (Table 1). This diagnostic uncertainty may lead to overdiagnosis of IE in patients with positive results of blood cultures (e.g., non-staphylococcal bacteremia) but inconclusive imaging results. Nonetheless, in the early phase of disease and suspicion of IE, it may be prudent to overdiagnose disease and perform echocardiography [5]. In the longer course of the disease, however, overtreatment of IE contributes to development of resistance of organisms in the microbiome and is associated with adverse events of antimicrobial agents [6]. An unprecise Duke minor criterion is, in our view, not helpful in the decision-making for or against the final diagnosis of IE.

The answers regarding what participants believed is true (knowledge question) and what they felt should be true (opinion question) were not similar on many of the questionnaires. On the one hand, these results may underline the difficulty in diagnosing IE in clinical practice, and on the other, they may point towards uncertainty in how to interpret and apply the Duke minor criterion of a predisposing heart condition. We only found an association between the wrong answers (very narrowly defined, Supplementary Material S2) with less than 3 years of clinical experience.

Two-thirds of the participants were convinced that in previous years, the diagnosis of MVP was overestimated. If this is true, a certain proportion of patients was falsely postulated to be at risk for IE. This again may have influenced the statistical risk stratification. A repetition of this study with current diagnostic methods may help to answer this question.


Bi-directional graph of Answers of Question 1 and 3
Knowledge Question
Opinion Question
80.00 60.00 40.00 20.00 0.00 -20.00 -40.00 -60.00 -80.00
Tumor
Paravalvular leakage
Low flow
Endothelial damage
Arrhythmias
Thrombus
Prior Myocardial infarction / coronary heart disease
Dilatative cardiomyopathy
Hypertrophic obstructive cardiomyopathy
Significant turbulence
Heart transplant
Heart failure
Cardiac surgery (without foreign body material)
Pulmonary valve stenosis
Degenerative valve disease
Tricuspid valve stenosis
Pulmonary valve insufficiency
Tricuspid valve insufficiency
Cyanotic heart disease
Mitral valve stenosis
Rheumatic heart disease
Aortic valve insufficiency
Aortic valve stenosis
Mitral valve prolapse
Mitral valve insufficiency
Bicuspid aortic valve
Shunt
Vitium (not specified)
Grown-up congenital heart disease
Valvular vitium
Prior Infective Endocarditis
-80.00 -60.00 -40.00 -20.00 0.00 20.00 40.00 60.00 80.00

◀**Fig. 1** Participants were asked what a predisposing heart condition for infective endocarditis includes (knowledge question) and what they felt should be listed as a predisposing heart condition (opinion questions). Results are presented in frequency percentages (%). Bi-directional graph to illustrate the accordance between knowledge and opinion

Our survey does not provide final results other than to show that there is a trend for uncertainty regarding what is encountered as a Duke minor criterion predisposing heart condition in a native valve. In our view, it is reasonable to encounter anatomical variants that cause significant turbulence and may be a risk factor when IE is suspected at first clinical presentation. However, over a 2-week period, the clinical course, microbiological criteria, and repeated imaging with modern techniques should allow confirmation or rejection of the definite diagnosis of IE in the majority of cases, irrespective of the presence of valve disease.

Our survey has limitations. It includes a selection bias of participants, because only physicians present at morning meetings at the date of investigation filled out the questionnaire. Although the questionnaire was tested on several occasions, it was not validated prior to the study.

CONCLUSION

Our survey shows that in clinical practice there is uncertainty regarding what is encountered as a Duke minor criterion predisposing heart condition in a native valve. As has been done for the term "predisposing heart condition" with respect to antimicrobial prophylaxis, a more precise definition for diagnosis of IE would be helpful. A meta-analysis investigating the statistical association between predisposing heart conditions in native valves and IE is currently being performed.

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Switzerland; Clinic of Cardiology, Kantonsspital, Olten, Switzerland; Division of Cardiology, Department of Internal Medicine, Kantonsspital Winterthur, Winterthur, Switzerland; Department of Internal Medicine, Spitäler FMI, Interlaken, Interlaken, Switzerland; Department of Internal Medicine, Regionalspital Emmental, Burgdorf, Burgdorf, Switzerland; Department of Internal Medicine, Regionalspital Emmental, Langnau, Langnau i.E., Switzerland; Division of Infectious Diseases and Hospital Epidemiology, Kantonsspital Baselland, University of Basel, Basel, Switzerland; Division of Infectious Diseases and Department of Cardiology, Luzerner Kantonsspital, Lucerne, Switzerland.

Compliance with Ethics Guidelines. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013.

Disclosures. Annina E. Büchi, Mario Hoffmann, Stephan Zbinden, and Parham Sendi all have nothing to disclose.

Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

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